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RAW SEQUENCE LISTING DATE: 02/12/2002 PATENT APPLICATION: US/09/813,271B TIME: 08:59:40

Input Set: N:\Crf3\02062002\I813271B.raw
Output Set: N:\CRF3\02122002\I813271B.raw

SEQUENCE LISTING

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3 (1) GENERAL INFORMATION:
      4
             (i) APPLICANT: Nico Cerletti
            (ii) TITLE OF INVENTION: New process for the production of
      5
      6
                                      biologically active protein
           (iii) NUMBER OF SEQUENCES: 13
      7
      8
            (iv) CORRESPONDENCE ADDRESS:
      9
                  (A) ADDRESSEE: Novartis Patent Department
     10
                  (B) STREET: 564 Morris Avenue
     11
                  (C) CITY: Summit
     12
                  (D) STATE: New Jersey
     13
                  (E) COUNTRY: USA
     14
                  (F) ZIP: 07901
     15
             (V) COMPUTER READABLE FORM:
     16
                  (A) MEDIUM TYPE: Floppy disk
                  (B) COMPUTER: IBM PC compatible
     17
                  (C) OPERATING SYSTEM: PC-DOS/MS-DOS
     18
     19
                  (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)
     20
            (Vi) CURRENT APPLICATION DATA:
                  (A) APPLICATION NUMBER: US/09/813,271B
C--> 21
C--> 22
                  (B) FILING DATE: 20-Mar-2001
     23
           (vii) PRIOR APPLICATION DATA:
     24
                  (A) APPLICATION NUMBER: PCT/EP95/02719
     25
                  (B) FILING DATE: 12-Jul-95
     26
                  (A) APPLICATION NUMBER: EPO 94810439.3
     27
                  (B) FILING DATE: 25-Jul-94
          (viii) ATTORNEY/AGENT INFORMATION:
     28
     29
                  (A) NAME: Pfeiffer, Hesna J. .
     30
                  (B) REGISTRATION NUMBER: 22640
                  (C) REFERENCE/DOCKET NUMBER: 4-20039C/C1C1/USN
     31
     32
            (ix) TELECOMMUNICATION INFORMATION:
                  (A) TELEPHONE: (908) 522-6940
     33
                  (B) TELEFAX: (908) 522-6955
     34
        (2) INFORMATION FOR SEQ ID NO: 1:
     35
             (i) SEQUENCE CHARACTERISTICS:
     36
     37
                  (A) LENGTH: 339 base pairs
     38
                  (B) TYPE: nucleic acid
     39
                  (C) STRANDEDNESS: double
     40
                  (D) TOPOLOGY: linear
            (ii) MOLECULE TYPE: cDNA to mRNA
     41
     42
           (iii) HYPOTHETICAL: NO
           (vii) IMMEDIATE SOURCE:
     43
                  (B) CLONE: E. coli LC137/pPLMu.hTGF-betal (DSM 5656)
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(ix) FEATURE:
45
46
             (A) NAME/KEY: CDS
47
             (B) LOCATION: 1..336
48
             (D) OTHER INFORMATION:/product= "human TGF-beta1"
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
49
        GCC CTG GAC ACC AAC TAT TGC TTC AGC TCC ACG GAG AAG AAC TGC TGC
                                                                                  48
50
        Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys
51
52
        GTG CGG CAG CTG TAC ATT GAC TTC CGC AAG GAC CTC GGC TGG AAG TGG
                                                                                  96
53
        Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp
54
55
56
        ATC CAC GAG CCC AAG GGC TAC CAT GCC AAC TTC TGC CTC GGG CCC TGC
                                                                                 144
        Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys
57
58
                  35
                                      40
                                                           45
        CCC TAC ATT TGG AGC CTG GAC ACG CAG TAC AGC AAG GTC CTG GCC CTG
                                                                                 192
59
        Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu
60
                                                       60
61
             50
                                  55
                                                                                 240
        TAC AAC CAG CAT AAC CCG GGC GCC TCG GCG GCG CCG TGC TGC GTG CCG
62
        Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro
63
64
                              70
                                                   75
                                                                                 288
65
        CAG GCG CTG GAG CCG CTG CCC ATC GTG TAC TAC GTG GGC CGC AAG CCC
        Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro
66
                                               90
67
                          85
        AAG GTG GAG CAG CTG TCC AAC ATG ATC GTG CGC TCC TGC AAG TGC AGC
                                                                                 336
68
        Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser
69
70
                     100
                                          105
                                                                                 339
        TGA
71
   (2) INFORMATION FOR SEQ ID NO: 2:
        (i) SEQUENCE CHARACTERISTICS:
74
75
             (A) LENGTH: 112 amino acids
             (B) TYPE: amino acid
76
77
             (D) TOPOLOGY: linear
       (ii) MOLECULE TYPE: protein
78
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:
79
        Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys
80
81
                           5
        Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp
82
83
                                           25
84
        Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys
85
                  35
86
        Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu
87
                                  55
                                                       60
        Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro
88
89
        Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro
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                                               90
92
        Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser
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                     100
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95 (2) INFORMATION FOR SEQ ID NO: 3:
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	109					GCC													48
	110	Ala	Leu	_	Ala	Ala	Tyr	Cys		Arg	Asn	Val	GIn		Asn	Cys	Cys		
M>				115					120					125					
	112					TAC													96
	113	Leu	Arg	Pro	Leu	Tyr	Ile		Phe	Lys	Arg	Asp		Gly	Trp	Lys	\mathtt{Trp}		
M>	114		130					135					140						
	115					AAA													144
	116	Ile	His	Glu	Pro	Lys	Gly	Tyr	Asn	Ala	Asn.	Phe	Cys	Ala	Gly	Ala			
M>	117	145					150					155					160		
	118					AGT													192
•	119	Pro	Tyr	Leu	Trp	Ser	Ser	Asp	Thr	Gln	His	Ser	Arg	Val	Leu	Ser	Leu		
M>	120					165					170					175			
	121	TAT	AAT	ACC	ATA	AAT	CCA	GAA	GCĀ	TCT	GCT	TCT	CCT	TGC	TGC	GTG	TCC	7	240
	122	Tyr	Asn	Thr	Ile	Asn	Pro	Glu	Ala	Ser	Ala	Ser	Pro	Cys	Cys	Val	Ser		
W>	123				180	•				185					190				
	124					CCT												:	288
	125	Gln	Asp	Leu	Glu	Pro	Leu	Thr	Ile	Leu	Tyr	Tyr	Ile	Gly	Lys	Thr	Pro		
W>	126			195					200					205					
	127					CTT												:	336
	128	Lys	Ile	Glu	Gln	Leu	Ser	Asn	Met	Ile	Val	Lys	Ser	Cys	Lys	Cys	Ser		
W>	129		210					215					220						
	130	TAA																:	339
	132	(2) INFO	RMAT:	ION 1	FOR :	SEQ :	ID NO	O: 4	:										
	133	(i)	SEQ	UENC:	E CH	ARAC:	reri:	STIC	S:										
	134		(A) LE	NGTH	: 112	2 am:	ino a	acid	S									
	135		(B) TY	PE: a	amino	o ac	id											
	136		(D) TO	POLO	GY: 3	linea	ar											•
	137	(ii)	MOL	ECUL:	E TY	PE:]	prote	ein											
	138	(xi)	SEQ	UENC:	E DE	SCRI	PTIO	N: S	EQ I	D NO	: 4:								
	139	Ala	Leu	Asp	Ala	Ala	Tyr	Cys	\cdot Phe	Arg	Asn	Val	Gln	Asp	Asn	Cys	Cys		
	140	1		-		5	=	=			10					15			
	141	Leu	Arg	Pro	Leu	Tyr	Ile	Asp	Phe	Lys	Arg	Asp	Leu	Gly	Trp	Lys	Trp		
	142		, -		20	-		-		25		-		_	30	-	_		
	143	Ile	His	Glu	Pro	Lys	Gly	Tyr	Asn	Ala	Asn	Phe	Cys	Ala	Gly	Ala	Cys		
	144			35		-	-	-	40				-	45	-		-		
	145	Pro	Tvr	Leu	Trp	Ser	Ser	Asp	Thr	Gln	His	Ser	Arq	Val	Leu	Ser	Leu		
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	167	•) SEQ									mma	CAC	CAC	220	mcc	mcm.	48	0
	168		r TTG															40	5
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W>		14		GIU	FIU	цуз	150	ıyı	TYT	AIG	Non	155	Cys	Der	Gry	110	160		
M>	177		A TAC	CTC	CGC	λСΨ		CAC	מרמ	A C C	CAC		ACC.	СТС	CTC	GGA		19:	2
	178		o Tyr															1).	_
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	181		r Asn																•
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., .	183	CA	G GAC	CTG		CCC	CTG	ACC	ATC		TAC	ТАТ	GTT	GGG		ACC	CCC	288	8
	184		n Asp																_
W>		01		195					200		-1-	-1-		205	5				
	186	АА .	A GTG			CTC	TCC	AAC		GTG	GTG	AAG	TCT		AAA	TGT	AGC	330	6
	187		s Val																
W>		-1	210					215				-1-	220	-1-		- 4 -			
	189	TG.																339	9
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	192) SEQ																
	193	•			NGTH					s									
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	195				POLO														
	196	(ii) MOL	•															
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198		Leu	ASP	THI	ASII 5	TYL	Cys	Phe	AIG		ьеи	GIU	GIU	ASII	15	Cys	
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200	Val	Arg	PIO		TAT	тте	ASP	Pne		GIII	ASP	ьeu	СТУ		ьуѕ	пр	
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202	Val	His		Pro	ьys	GIŸ	туг	_	Ата	ASII	Pne	Cys		GIY	PLO	Cys	
203	D		35		a	31-	3	40	m la	77.5 -	O	mh	45	T	01	T	
204	PIO	Tyr	ьeu	Arg	ser	Ата	_	THE	THE	HIS	ser		Val	ьeu	GIY	ьeu	
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206	_	Asn	Thr	Leu	Asn		GIU	Ата	ser	Ala		Pro	Cys	Cys	val		
207	65	>	.	a 1	D	70	m 1	- 1-	T	М	75	*** 1	01	N	m	80	
208	GIN	Asp	ьеu	GIU		ьeu	Thr	шe	ьeu		Tyr	vaı	СТА	Arg		Pro	
209	*	**- 1	a 1	a 1	85	a		34-4	**- 1	90	T	a	a	.	95	a	
210	Lys	Val	Glu		Leu	ser	Asn	Met		vaı	ьуs	ser	Cys		Cys	ser	
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222		(B)	CL	ONE:	E. 0	coli	LC1	37/pI	PLMu	.TGF	-beta	al(44	4/45)beta	a 3		
223	(ix)	FEAT															
224	(ix)	(A)	NA1	ME/KI	EY: n	_	_	ide									
224 225	(ix)	(A)	NAI	ME/KI	ON:1	.132	2										
224 225 226	, ,	(A) (B) (D)	NAI LOC OTI	ME/KI CATIO HER	ON:1. INFOI	.132	2		duct:	= "N-	-teri	mina:	l 44	amiı	no		
224 225 226 227	acids of	(A) (B) (D) huma	NAI LOC OTI an TC	ME/KI CATIO HER I GF-bo	ON:1. INFOI	.132	2		luct=	= "N·	-teri	mina	1 44	amiı	no		
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224 225 226 227 228 229	acids of	(A) (B) (D) huma FEAT	NAI LOC OTI IN TO TURE NAI	ME/KI CATIO HER I GF-bo : ME/KI	ON:1. INFOI etal' EY: n	.132 RMAT] '	ON:,	/prod	iuct=	= "N·	-teri	mina.	l 44	amiı	no		
224 225 226 227 228 229 230	acids of	(A) (B) (D) huma FEAT (A)	NAI LOC OTI IN TO TURE NAI LOC	ME/KICATION HER IN GF-box HE/KICATION	ON:1. INFOI etal' EY: n ON:13	132 RMATI nat_r	ION:, pept:	/prod									
224 225 226 227 228 229 230 231	acids of	(A) (B) (D) huma FEAT (A) (B)	NAI LOC OTI IN TO FURE NAI LOC OTI	ME/KI CATIO HER I GF-be HE/KI CATIO HER I	ON:1. INFOI etal' EY: n ON:13	132 RMATI nat_p 333	ION:, pept:	/prod									
224 225 226 227 228 229 230 231 232	acids of (ix)	(A) (B) huma FEAT (A) (B) huma) NAI) LOO) OTI TURE) NAI) LOO) OTI	ME/KI CATIO HER : GF-be: CATIO HER : CATIO HER : GF-be:	ON:1. INFOI etal' EY: n ON:13	132 RMATI nat_p 333	ION:, pept:	/prod									
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224 225 226 227 228 229 230 231 232 233 234 235 236 237 238	acids of (ix) acids of (ix) TGF-beta (xi)	(A) (B) (D) huma (A) (B) (D) huma FEAT (A) (B) (D) 1-3" SEQU	NAI LOC TURE NAI LOC TURE NAI LOC TURE NAI LOC TURE NAI	ME/KI CATIO HER : GF-be CATIO HER : ME/KI CATIO HER : ME/KI CATIO HER :	ON:1 INFOI EY: n ON:13 INFOI Eta3' EY: (ON:1 INFOI	nat_r mat_r 333 RMATI	pept: 336 ION:, ION:,	/prod ide /prod /prod	duct:	= "C: = "hy : 7:	-tern	mina:	l 68 F-be	amin	no amed		
224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239	acids of (ix) acids of (ix) TGF-beta (xi) GCC	(A) (B) (D) huma (A) (B) (D) huma FEAT (A) (B) (D) 1-3" SEQU CTG) NAI) LOC TURE) NAI) LOC TURE) NAI) LOC TURE) NAI) LOC) OTI	ME/KICATION HER INTERPORT TO THE	ON:1 INFOI etal' EY: m ON:1 INFOI eta3' EY: (ON:1 INFOI SCRII AAC	nat_r nat_r S333 CDS336 RMATI	pept: 336 ION:, 6 ION:, N: SI	/prod ide /prod /prod EQ II	luct= luct= O NO AGC	= "C- = "hy : 7: TCC	-tern ybrid	mina: d TG	l 68 F-be	amin ta na	no amed TGC		48
224 225 226 227 228 229 230 231 232 233 234 235 237 238 239 240	acids of (ix) acids of (ix) TGF-beta (xi) GCC Ala	(A) (B) (D) huma (A) (B) (D) huma FEAT (A) (B) (D) 1-3" SEQU) NAI) LOC TURE) NAI) LOC TURE) NAI) LOC TURE) NAI) LOC) OTI	ME/KICATION HER INTERPORT TO THE	ON:1 INFOI etal' EY: n ON:13 INFOI eta3' EY: C ON:1 INFOI SCRII AAC Asn	nat_r nat_r S333 CDS336 RMATI	pept: 336 ION:, 6 ION:, N: SI	/prod ide /prod /prod EQ II	luct= luct= O NO AGC	= "C = "hy : 7: TCC Ser	-tern ybrid	mina: d TG	l 68 F-be	amin ta na	no amed TGC Cys		48
224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241	acids of (ix) acids of (ix) TGF-beta (xi) GCC Ala 1	(A) (B) huma FEAT (A) (B) huma FEAT (A) (B) (D) huma CTG Leu) NAI) LOC) OTI TURE) NAI) LOC) OTI TURE) NAI) LOC) OTI GAC ASP	ME/KICATION HER INTERPORT TO THE TO THE	ON:1 INFOI etal' EY: m ON:13 INFOI eta3' EY: C ON:1 INFOI SCRII AAC Asn	nat_r , , , , , , , , , , , , , , , , , , ,	pept: 336 ION:, ION:, TGC	/prod /prod /prod TTC Phe	duct= luct= O NO AGC Ser	= "C = "hy : 7: TCC Ser 10	ybric ACG Thr	nina: d TG: GAG Glu	l 68 F-bet AAG Lys	amin ta na AAC Asn	no TGC Cys 15	Cys	
224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242	acids of (ix) acids of (ix) TGF-beta (xi) GCC Ala 1 GTG	(A) (B) huma FEAT (A) (B) huma FEAT (A) (CTG Leu CGG	NAI LOC OTH TURE NAI LOC OTH TURE NAI LOC OTH GAC ASP	ME/KICATION HER IN THE SET - DO SET IN THE S	ON:1 INFOI EY: INFOI EY: ON:1 INFOI EY: O ON:1 INFOI SCRII AAC ASD TAC	nat_E 333 RMATI	pept: 336 ION:, 5 ION:, TGC Cys	/prod /prod /prod TTC Phe	duct= luct= O NO AGC Ser CGC	= "C' = "hy : 7: TCC Ser 10 AAG	-terrybric ACG Thr GAC	mina d TG GAG Glu CTC	l 68 F-bet AAG Lys GGC	amin ta na AAC Asn TGG	TGC Cys 15 AAG	Cys TGG	48 96
224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 240 241 242 243	acids of (ix) acids of (ix) TGF-beta (xi) GCC Ala 1 GTG	(A) (B) huma FEAT (A) (B) huma FEAT (A) (B) (D) huma CTG Leu	NAI LOC OTH TURE NAI LOC OTH TURE NAI LOC OTH GAC ASP	ME/KICATION HER IN THE ME/KICATION ME/KICATION HER IN THE ME/KICATIO	ON:1 INFOI EY: INFOI EY: ON:1 INFOI EY: O ON:1 INFOI SCRII AAC ASD TAC	nat_E 333 RMATI	pept: 336 ION:, 5 ION:, TGC Cys	/prod /prod /prod TTC Phe	duct= O NO AGC Ser CGC Arg	= "C' = "hy : 7: TCC Ser 10 AAG	-terrybric ACG Thr GAC	mina d TG GAG Glu CTC	l 68 F-bet AAG Lys GGC	amin AAC Asn TGG Trp	TGC Cys 15 AAG	Cys TGG	
224 225 226 227 228 230 231 232 233 234 235 236 237 238 240 241 242 243 244	acids of (ix) acids of (ix) TGF-beta (xi) GCC Ala 1 GTG Val	(A) (B) (D) huma (A) (B) (D) huma FEAT (A) (B) (CTG Leu CGG Arg	NAI LOG	ME/KICATION HER IN THE ME/KICATION ME/KICATION HER IN THE ME/KICATIO	ON:1 INFOI EY: INFOI EY: ON:1 INFOI EX: ON:1 INFOI AAC ASI TAC TYT	MATE MATE MATE MATE CDS MATE CTION TAT TYT ATT Ile	pept: 336 ION:, TGC Cys GAC Asp	/prod /prod /prod TTC Phe TTC	duct= O NO AGC Ser CGC Arg 25	= "C = "hy : 7: TCC Ser 10 AAG Lys	ACG Thr GAC Asp	d TG GAG Glu CTC Leu	l 68 F-bet AAG Lys GGC Gly	amin AAC Asn TGG Trp 30	TGC Cys 15 AAG Lys	Cys TGG Trp	96
224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 240 241 242 243	acids of (ix) acids of (ix) TGF-beta (xi) GCC Ala 1 GTG Val ATC	(A) (B) huma FEAT (A) (B) huma FEAT (A) (CTG Leu CGG	NAI LOC OTI TURE NAI LOC OTI TURE NAI LOC OTI UENCI GAC ASP CAG GIN	ME/KICATION HER IN THE	ON:1 INFOI EY: IT ON:13 INFOI EX: CON:1 INFOI AAC ASI TAC TYT AAG	MATE MATE MATE MATE MATE CDS MATE CDS MATE TAT TYT ATT Ile GGC	pept: 336 ION:, TGC Cys GAC Asp	/prod	duct= O NO AGC Ser CGC Arg 25 GCC	= "C' = "hy : 7: TCC Ser 10 AAG Lys	ACG Thr GAC Asp	mina d TG GAG Glu CTC Leu TGC	l 68 F-bet AAG Lys GGC Gly TCA	amin ta na AAC Asn TGG Trp 30 GGC	TGC Cys 15 AAG Lys	Cys TGG Trp TGC	

VERIFICATION SUMMARY

DATE: 02/12/2002 TIME: 08:59:41 PATENT APPLICATION: US/09/813,271B

Input Set : N:\Crf3\02062002\1813271B.raw Output Set: N:\CRF3\02122002\I813271B.raw

L:21 M:220 C: Keyword misspelled or invalid format, [(A) APPLICATION NUMBER:] L:22 M:220 C: Keyword misspelled or invalid format, [(B) FILING DATE:] L:111 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:114 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:117 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:120 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:123 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:126 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:129 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3 L:170 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5 L:173 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5 L:176 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5 L:179 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5 L:182 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5 L:185 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5 L:188 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:5